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A profile of neuropsychiatric problems and their relationship to quality of life for Parkinson's disease patients without dementia

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Abstract

Neuropsychiatric problems are common in Parkinson's disease (PD) but there is little information regarding how they impact on quality of life. PD patients without dementia (49) were assessed for low mood/depression, fatigue, apathy, sleep problems and hallucinations. Measures of quality of life and motor function were also obtained. Over 77% of the patients reported symptoms consistent with one or more neuropsychiatric problems. Low mood/depression, anxiety and the presence of hallucinations predicted poorer quality of life after controlling for motor symptoms. Additional to the motor symptoms, we found that specific neuropsychiatric problems may impact on quality of life for PD patients.

Keywords: Parkinson's disease; Quality of life-PDQ; Depression; Anxiety; Fatigue; Apathy

1. Introduction

A range of neuropsychiatric problems have been associated with Parkinson's disease (PD) in the absence of dementia. Individual symptoms, such as depression, are linked to reduced independence and quality of life for PD patients [1,2], and are important predictors of caregiver distress which may result in early rest home placement [3]. However, these symptoms are often not recognized by treating physicians [4]. Varying prevalence rates have been reported for neuropsychiatric symptoms in PD patients depending on methodology, with up to 70% reporting symptoms consistent with depression [5], 40% for anxiety [6], 30% hallucinations [7], 43% apathy [6,8], 40% fatigue [9] and 80% for sleep problems [10,11].

Although the presence of individual neuropsychiatric symptoms has been well documented, relatively little is known regarding a typical profile associated with PD without dementia. Aarsland and Karlsen [12] examined the frequency of neuropsychiatric symptoms in a group of 139 PD patients (Hoehn & Yahr, (H&Y) stages I–IV) with the Neuropsychiatric Inventory [13], and found depression (38%) and hallucinations (27%) to be the most common disorders, with 61% of the sample reporting at least one symptom. Psychiatric symptoms were more common among patients in rest homes and those with cognitive impairment. However, 42% of their sample either met the criteria for or had questionable dementia and more recent studies indicate that PD patients with dementia have a greater number of neuropsychiatric problems [14]. Shulman et al. [9] reported sleep disturbance (47%) and sensory symptoms (63%) as being the most common neuropsychiatric problems in a group of 99 PD patients (H&Y I–IV) without dementia. High rates of fatigue (40%), depression (36%) and anxiety (33%) were also reported. Shulman et al. [9] also found comorbidity to be high, with 59% of the patients having two or more symptoms and 25% having four or more.

Neuropsychiatric problems have been found to contribute to the reduction in quality of life in PD patients, in addition to the motor symptoms associated with the disease [1,15]. However, no prior study has used a single group of subjects to examine the effect that different

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neuropsychiatric problems have on quality of life for PD patients.

Thus, the major goal of the present research was to examine the relationship between different neuropsychiatric problems and quality of life. A related aim was to determine the profile of neuropsychiatric symptoms in this group. Because many problems such as apathy, fatigue, depression and sleep disturbance have a considerable degree of symptom overlap, we also examined the relationships among the different neuropsychiatric measures.

2. Methods

Approval for the study was granted by the Upper South B Regional Ethics Committee and informed consent was obtained from patients with a diagnosis of idiopathic PD confirmed by a specialist neurologist. Inclusion criteria were as follows: no evidence of another major medical illness, no evidence of dementia (MMSE$\geqslant$25) [16], and less than 80 years of age. Of the 115 letters that were mailed, 11/115 (9.6%) could not participate due to illness or dementia, 8/115 (6.9%) were deceased, 8/115 (6.9%) declined and 34/115 (29.6%) did not respond. Fifty-four patients who met the inclusion criteria (31 males and 18 females) volunteered to take part. Of these, five did not complete the take home tests and were excluded. The clinical and demographic characteristics of the 49 patients included in this study are shown in Table 1.

2.1. Procedure

Information regarding current cognitive status, motor symptoms, hallucination, sleep problems and depression were all collected during the session. Patients were also asked to take home and complete questionnaires which assessed symptoms of apathy, fatigue and anxiety. Details regarding how to complete the forms were explained during the session. Any questions or difficulties were addressed when they were returned 1 week later.

2.1.1. Instruments used to collect clinical characteristics

(1) A semi-structured interview was used to gather demographic and clinical details and included information about patient health history, substance abuse, age and duration of PD.
(2) Motor impairments were assessed for all patients using the Unified Parkinson's Disease Rating Scale (UPDRS) [17]. Three scores were generated using this scale: (a) severity of motor symptoms rated using Section 3, (b) tremor score (calculated as the average of items 16 and 20–26) and (c) non-tremor score (calculated as the average of items 5, 7, 12–15, 18, 19 and 27–44) as outlined by Lewis et al. [18].
(3) The H&Y was used to rate the stage of the disease [19].
(4) Overall functional status was evaluated using the Modified Schwab and England Activities of Daily Living Scale (S&E) [20]. The majority of patients in this study were independent in daily living. Only two patients scored below 70% (both 60%) and one scored 30%. In each of these cases, the low scores reflected severe motor disruption.

2.1.2. Instruments used to collect neuropsychiatric information

(1) Frequency of sleep disturbance was assessed using a single screening item contained in the UPDRS [17]. Patients were asked to respond with yes/no to the question, "Do you have any problems with your sleep?"
(2) The presence of hallucinations were assessed using the UPDRS which uses a five-point scale where 0 = none, 1 = vivid dreaming, 2 = "benign" hallucinations with insight retained, 3 = occasional to frequent hallucinations or delusions without insight, 4 = persistent hallucinations, delusions or florid psychosis [17]. For the purposes of this study, hallucinations were considered to be present if the patient scored greater than two.
(3) Symptoms of depression were assessed using the Beck Depression Inventory (BDI-II) [21] which consists of 21 items, rated from 0 to 3 with a maximum possible score of 63. A score of $\geqslant$9 was taken as evidence of low mood/depression [22].
(4) Anxiety was assessed using seven items from the Hospital Anxiety and Depression Scale (HADS). Each was rated on a four-point scale (0–3) with a maximum score of 21 [23]. A score of $\geqslant$8 was taken as evidence of anxiety.
(5) Fatigue was assessed using the Fatigue Severity Scale (FSS) which consists of nine items, each scored on a seven-point scale where one indicates "strongly disagree" and seven "strongly agree". We modified the questionnaire so that mental fatigue and physical fatigue could be examined separately. Patients were asked to answer each item separately for both mental and physical fatigue. Average scores were then calculated. A cut-off of $>$4, which has previously been used for patients with PD, was used for both scores to indicate presence of mental or physical fatigue [9].
(6) Apathy was assessed using the Apathy Scale (AS) [6] (14 item self-report measure rated 0–4 with a maximum score of 56). Higher scores were indicated more symptoms of apathy. We used the recommended cut-off of $>$14 [6].

Table 1
Clinical and demographic characterstics, Parkinson's disease patients

		Mean (SD)		Range		
Age		66.5 (6.8)		52.0–770		
MMSE[a]		28.6 (1.3)		25.0–300		
PD onset[b]		6.0 (4.2)		0.3–23.0		
UPDRS[c]		29.6 (9.7)		13.0–53.0		
Tremor score		0.6 (0.4)		0.0–1.9		
Non-tremor score		1.2 (0.4)		0.5–2.6		
S&E[d]		81.5% (0.1)		30.0%–100.0%		
H&Y stage[e]	1 (n = 9)	1.5 (n = 6)	2 (n = 10)	2.5 (n = 13)	3 (n = 8)	4 (n = 3)

[a]Mini Mental Status Exam.
[b]Number of years since onset of Parkinson's disease symptoms.
[c]Unified Parkinson's Disease Rating Scale (motor score component).
[d]Modified Schwab and England Activities of Daily Living Scale.
[e]Hoehn and Yahr.

2.1.3. Measure used to evaluate quality of life

Quality of life was assessed using the Parkinson's disease questionnaire (PDQ-39) [24], a 39 item self-report questionnaire developed to assess the impact of PD on an individual's daily life. The questionnaire contains eight dimensions, each scored from 0 (no problems at all) to 100 (maximum level of problems) using the formula supplied in the manual. A single index score was calculated by averaging the eight scale scores.

2.2. Statistical analysis

The percentage of individuals with neuropsychiatric problems was calculated using previously validated cut-offs where possible. Quantitative data are also reported in terms of means and standard deviations. Pearson correlation was employed to assess the relationship among the different neuropsychiatric problems and also between clinical/demographic characteristics and neuropsychiatric problems. Hierarchical multiple regressions were used to assess the influence of motor impairment and neuropsychiatric problems on quality of life.

3. Results

Table 2 displays the mean and standard deviation for the entire sample and also percentage of patients who exceeded the cut-offs for each of the seven neuropsychiatric outcomes. Overall, neuropsychiatric problems were extremely common with over 77% of the sample reaching the cut-off for one or more problems (11/49 = 0; 6/49 = 1; 9/49 = 2; 14/49 = 3; 2/49 = 4 and 4/49 = 5). Physical fatigue, mental fatigue, low mood/depression and apathy were the most frequent neuropsychiatric problems, and were each reported by over 38% of the patients. Sleeping problems were reported by 32% of the patients. Anxiety and hallucinations were less frequent, with just over 16% and 12%, respectively, of the patients meeting the criteria for these symptoms.

One of our goals was to assess the relationship between the different neuropsychiatric problems because there is considerable symptom overlap. As can be seen from Table 3, there was a strong positive correlation between physical and mental fatigue. There were also significant positive relationships between physical fatigue, low mood/depression anxiety and apathy. Low mood/depression was significantly associated with anxiety, apathy and hallucinations. By contrast, mental fatigue and hallucinations were only significantly correlated with low mood/depression, and there was no significant association between sleep disturbance and any of the other measures.

We also examined the association between clinical/demographic characteristics and neuropsychiatric outcomes. As can be seen from Table 4, fatigue and apathy scales and the presence of hallucinations were positively correlated with non-tremor scores derived from the UPDRS and S&E for activities of daily living. Fatigue and hallucinations were also associated with motor stage; using the H&Y. Sleep problems were positively correlated only with disease duration. There was no association between scores of low mood/depression or anxiety on any of the clinical or demographic characteristics and no significant association with age or gender for any neuropsychiatric outcome.

Hierarchical multiple regression analyses were used to examine the influence of motor impairment and neuropsychiatric problems on quality of life (PDQ-39). Specifically, we planned to test whether neuropsychiatric problems made an independent contribution to predicting quality of life, after controlling for the relationship between motor symptoms and quality of life. To reduce collinearity, we used a single measure of fatigue (the average of scores for mental and physical fatigue), and only the tremor and non-tremor UPDRS scores were included as measures of motor symptoms. Scores for each PDQ-39 domain, as well as the overall score, were used as dependent variables. For each dependent variable, motor symptoms were entered on the first step, and each neuropsychiatric symptom was then entered separately on the second step. Beta weights for tremor and non-tremor scores from the first step, and for each neuropsychiatric symptom on the second step, are listed in Table 5. Also shown is the incremental variance accounted for PDQ-39 scores by the each neuropsychiatric symptom (R^2 change). Table 5 shows that non-tremor scores, but not tremor scores, were significantly related to overall quality of life (PDQ-Total). Among neuropsychiatric problems, anxiety, depression and the presence of hallucinations explained significant amount of variance after controlling for motor symptoms.

Table 5 shows that whereas non-tremor scores were significantly related to quality of life for all domains except stigma, tremor scores were not. Neuropsychiatric

Table 2
Mean, standard deviations and percentage of patients with problems for each neuropsychiatric measure

Maximum possible score in brackets	Mean (SD) for total group	Percentage (*n*) with problems	Range
Physical fatigue (7)	3.9 (1.6)	40.1 (20/49)	1.0–6.9
Mental fatigue (7)	3.7 (1.6)	38.8 (19/49)	1.0–7.0
Low mood/depression (63)	7.9 (5.0)	40.1 (20/49)	0.0–19.0
Anxiety (21)[a]	5.1 (3.6)	16.7 (7/42)	0.0–17.0
Apathy (42)	11.9 (5.9)	38.8 (19/49)	0.0–25.0
Hallucinations	N/A[b]	10.2 (5/49)	N/A[b]
Sleep disturbance	N/A[b]	32.7 (16/49)	N/A[b]

[a]The Hospital Anxiety and Depression Scale (HADS) used to detect the presence of anxiety was only completed by 42 of the 49 patients.
[b]N/A, not applicable; these measures used a single yes/no format.

Table 3
Correlations between different neuropsychiatric measures

	Physical fatigue	Mental fatigue	Low mood/depression	Anxiety	Apathy	Hallucinations	Sleep disturbance
Physical fatigue	–						
Mental fatigue	0.80***	–					
Low mood/depression	0.36*	0.30*	–				
Anxiety[a]	0.32*	0.24	0.67**	–			
Apathy	0.30*	0.28	0.40**	0.24	–		
Hallucinations	0.19	0.12	0.32*	0.29	0.18	–	
Sleep disturbance	0.09	0.11	0.10	0.26	0.19	0.11	–

[a]The Hospital Anxiety and Depression Scale (HADS) used to detect the presence of anxiety was only completed by 42 of the 49 patients.
*$p<0.05$.
**$p<0.01$.
***$p<0.001$.

Table 4
Correlations for clinical/demographic characteristics and neuropsychiatric problems

	Physical fatigue	Mental fatigue	Hallucinations	Apathy	Sleep problems	Low mood/depression	Anxiety
Gender	−0.08	−0.22	0.04	−0.26	−0.79	−0.02	−0.15
Age	0.12	0.05	−0.05	−0.13	−0.13	−0.17	−0.05
Disease duration[a]	0.10	0.26	−0.20	−0.07	0.37*	−0.16	0.10
H&Y[b]	0.43**	0.45**	0.49***	0.25	0.07	0.15	0.13
UPDRS[c]	0.40**	0.33*	0.30*	0.31*	−0.05	0.08	0.03
Tremor score	0.26	0.16	−0.00	0.15	0.01	−0.06	0.07
Non-tremor score	0.42**	0.40**	0.46***	0.35*	−0.01	0.20	0.07
S&E[d]	−0.39**	−0.39**	−0.58***	−0.40**	−0.02	−0.27	−0.07

[a]Number of years since diagnosis of Parkinson's disease.
[b]Hoehn and Yahr stage.
[c]Unified Parkinson's disease Rating Scale (motor score component).
[d]Modified Schwab and England Activities of Daily Living Scale.
*$p<0.05$.
**$p<0.01$.
***$p<0.001$.

Table 5
Beta weights and for tremor, non-tremor and each neuropsychiatric symptom for regression analyses predicting Parkinson's disease quality of life questionnaire

PDQ-Total	PD motor		Neuropsychiatric symptoms					
	Tremor	Non-tremor	Anxiety[a]	Apathy	Fatigue	Depression	Sleep	Hallucinations
	0.06	0.61***	0.69*** (0.46)	0.22 (0.04)	0.22 (0.04)	0.51** (0.23)	0.17 (0.02)	0.39** (0.10)
Subscales								
Mobility	−0.10	0.71***	0.43** (0.18)	−0.02 (0.00)	−0.01 (0.03)	0.28* (0.07)	−0.03 (0.00)	0.20 (0.03)
Activities of daily living	0.14	0.60***	0.36** (0.12)	0.30* (0.08)	0.28* (0.06)	0.25* (0.06)	0.21 (0.04)	0.30* (0.07)
Emotion	0.03	0.33*	0.78** (0.60)	0.21 (0.04)	0.20 (0.03)	0.66*** (0.41)	0.13 (0.02)	0.45** (0.16)
Stigma	0.14	0.11	0.45** (0.20)	0.21 (0.04)	0.04 (0.00)	0.34* (0.11)	0.14 (0.02)	0.24 (0.05)
Social support	0.15	0.36*	0.40** (0.16)	0.14 (0.02)	0.24 (0.05)	0.26 (0.06)	0.14 (0.02)	0.10 (0.00)
Cognitive impairment	0.23	0.48***	0.57*** (0.32)	0.33** (0.09)	0.35** (0.09)	0.42*** (0.16)	0.03 (0.00)	0.38** (0.11)
Communication difficulties	0.07	0.49***	0.37* (0.14)	0.40** (0.14)	0.09 (0.00)	0.28* (0.08)	0.23 (0.05)	0.28 (0.06)
Bodily discomfort	0.03	0.39**	0.47** (0.22)	0.05 (0.00)	0.27 (0.06)	0.28* (0.08)	0.20 (0.04)	0.39** (0.12)

R^2 change for each symptom is shown in parentheses.
[a]Only 42 patients completed the anxiety scale.
*$p<0.05$.
**$p<0.01$.
***$p<0.001$.

symptoms also explained significant variance in different domains of quality of life. Anxiety was significantly related to all of the PDQ-39 domains, after controlling for motor symptoms. A similar finding was evident for depression, which also accounted for significant incremental variance in quality of life scores for all domains except for perception of social support. Presence of hallucinations accounted for significant variance in the domains of daily living, emotional well-being, cognitive impairment and bodily discomfort.

By contrast, apathy was only significantly related to communication difficulties, cognitive impairment and the perception of cognitive impairment and fatigue with activities of daily living and cognitive impairment after controlling for motor symptoms. Sleep difficulties were only related to cognitive impairment. Overall, these results show that neuropsychiatric problems are associated with significant variance in quality of life for PD patients after controlling for the effects of motor symptoms.

4. Discussion

Our data suggest that neuropsychiatric problems are common for patients with PD. Over 77% of the patients reported symptoms consistent with at least one problem and more than 46% with three or more problems. Symptoms consistent with low mood/depression, physical fatigue, mental fatigue, apathy, and sleep problems were each reported by over 30% of the patients. Anxiety and hallucinations were relatively less common. Given the overlap between symptoms for these disorders we also examined the relationship between the different neuropsychiatric problems. Physical fatigue and low mood/depression were related to most other neuropsychiatric problems, with the exception of sleep disturbance. By contrast, the presence of hallucinations was only associated with depression, and there was no significant correlation between sleep disturbance and any of the other measures.

In terms of associations between clinical/demographic and neuropsychiatric problems, age and gender were not related to any of the neuropsychiatric problems. Motor scores were significantly related to increased fatigue, hallucinations and apathy. When motor scores were divided into tremor and non-tremor scores, significant associations were obtained for non-tremor scores only.

We also found that in addition to motor deficits, specific neuropsychiatric problems contributed to reduced quality of life in patients with PD. Anxiety, depression and the presence of hallucinations were significantly associated with an overall poorer quality of life, after controlling for motor symptoms. When different aspects of quality of life were considered separately, anxiety was always predictive of poorer quality of life. Similarly, depression and non-tremor scores were associated with poorer quality of life for every domain apart from the level of social support and stigma. In contrast, fatigue and increased sleep problems were only associated with increased cognitive impairment, and apathy was associated with increased self-ratings of cognitive impairment and communication difficulties.

Our results are consistent with other studies, which have reported similar levels of depression, fatigue and sleep disturbance in PD patients [8,9,25,26]. The prevalence of anxiety was somewhat lower here than in previous studies [9]. However, our study used the HADS while Shulman et al. [9] used the Beck Anxiety Scale [4], and there is currently no information regarding the relative sensitivity of these two measures with PD patients.

Our finding that tremor scores but not non-tremor scores were related to neuropsychiatric outcomes and poorer quality of life has also previously been reported [26,27]. Moreover, non-tremor scores have been found to predict poorer outcomes in terms of cognitive functioning [28], and it has been suggested that people with predominantly bradykinetic-rigid symptoms may represent a distinct clinical subgroup who have a more aggressive form of the disease with generally poorer cognitive outcomes [28].

Neuropsychiatric problems are increasingly recognized as contributing to poorer quality of life in patients with PD [1,29,30]. Fortunately, many of the neuropsychiatric problems associated with PD may be ameliorated with appropriate intervention. For example, recent research has piloted patient education regarding information on problems associated with degenerative disease. This research was shown to be beneficial to patients with PD and their caregivers [31].

It is important to acknowledge some possible limitations of our study. Unfortunately, the UPDRS provides only one item for sleep problems and the presence of hallucinations, resulting in no information regarding the type of sleep problem (onset, maintenance or duration) or hallucination (auditory or tactile) that was being experienced. Moreover, the question in the UPDRS relating to hallucinations encourages the reporting of only visual hallucinations, which may have led to an under-reporting of this problem. Although we endeavored to recruit a representative sample, only patients who volunteered were included, and thus it is possible that they were healthier than those who did not respond. Also, we restricted our inclusion criteria to those patients who did not have another major health problem. Arguably, both of these factors may have limited the representativeness of the sample. Nevertheless, our results still demonstrate that for many PD patients, neuropsychiatric problems as well as motor symptoms may contribute to reduced quality of life.

The identification of neuropsychiatric problems in patients with PD is important because these problems are amenable to treatment, and a lack of timely intervention may needlessly reduce the individuals' quality of life. Given that neuropsychiatric problems are not consistently associated with motor impairments, all patients should routinely be screened for commonly occurring problems such as anxiety, depression and fatigue.

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